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Jane A. Walker
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January 12, 2004
Date

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex Parte Gassenmeier et al.
Appeal No. _____

Applicant: Gassenmeier et al.
Serial Number: 09/800,624
Filed: March 7, 2001
Confirmation No.: 7473
Art Unit: 1761
Examiner: Wong, Leslie A.
Title: **ORGANOLEPTIC COMPOSITIONS: USE OF 3-MERCAPTO
ALKANOIC ACID ESTERS AS FLAVOR INGREDIENTS**
Attorney Ref. No.: GRISA-710

Cincinnati, Ohio 45202

January 12, 2004

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF TRANSMITTAL

Transmitted herewith, in triplicate, is the APPEAL BRIEF in this application, with respect to the Notice of Appeal filed on November 14, 2003.

Enclosed is a check in the amount of \$330.00 for the filing of this Brief.
Should any further fees be indicated herein, authorization is given to charge or credit
any overpayment to Deposit Account No. 23-3000.

Respectfully submitted,

WOOD, HERRON & EVANS, L.L.P.

By Beverly A. Lyman
Beverly A. Lyman, Ph.D.
Reg. No. 41,961

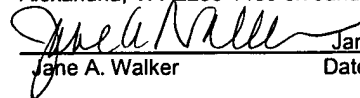
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BRIEF ON APPEAL

This is an appeal from the decision of the Examiner in a final Office Action dated May 19, 2003 (Paper No. 13). The pending rejected claims appear in the Appendix.

Real Party in Interest

The subject application is owned by Givaudan SA, Vernier, Switzerland.

Related Appeals and Interferences

None.

Status of the Claims

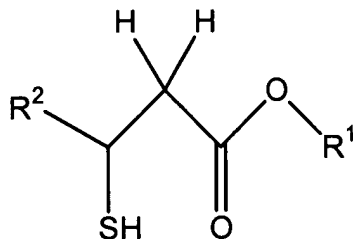
All pending claims 1-16 as listed in the Appendix are finally rejected under 35 U.S.C. § 103(a) over GB Patent 1 409 209 in view of Ashurst, Ed., Food Flavorings, Second edition, Blackie Academic & Professional, New York, 1995, pages 155-157. All pending claims 1-16 are appealed.

Status of Amendments

There are no amendments subsequent to the final office Action.

Summary of the Invention

A flavor or fragrance composition having at least one compound of formula I



which is a 3-mercaptoalkanoic acid ester, where R¹ is a branched or unbranched alkyl, alkenyl or alkadienyl group of C₁₋₈, and R² is methyl or ethyl, or a precursor, is disclosed (page 3, lines 9-14). Methods of flavoring or fragancing products with these compositions are also disclosed (page 4, lines 8-15). While 3-mercaptoalkanoic acid

esters are known compounds (page 7, lines 4-11), their organoleptic properties had not previously been realized (page 7, lines 12-16). Thus, the claimed flavor or fragrance composition containing these specific 3-mercaptoalkanoic acid esters, and method of flavoring or fragrancng using the composition, was inventive (page 5, line 9 to page 6, line 1).

Issue

Whether claims 1-16 are obvious under 35 U.S.C. § 103(a) over GB Patent 1 409 209 (hereinafter referred to as "Chiba") in view of Ashurst, Ed., Food Flavorings, Second edition, Blackie Academic & Professional, New York, 1995, pages 155-157 (hereinafter referred to as "Ashurst").

Grouping of Claims

The rejected claims stand and fall together.

Argument

The Examiner finds that Chiba discloses the claimed compounds, but not the specific use of the compounds as flavoring agents. The Examiner finds Ashurst discloses the well-known use of mercaptans as flavoring agents, and that it would be obvious to one skilled in the art to use Chiba's compounds as flavorants because the use of mercaptans as flavoring agents is conventional, as Ashurst teaches.

Applicants disagree with the Examiner because (1) one skilled in the art of flavor or fragrance compositions and methods would not look to Chiba, which discloses a method of preparing mercaptocarboxylic acid esters for industrial synthesis starting materials; (2) there is no motivation to combine Chiba with Ashurst because Chiba does

not teach or suggest any flavor or fragrance properties of mercaptocarboxylic acid esters, while Ashurst does not teach or suggest 3-mercaptoalkanoic acid esters at all; and (3) even if Chiba were combined with Ashurst, there is no reasonable expectation of success that it would yield 3-mercaptoalkanoic acid ester flavor or fragrance compositions, one reason being the known malodorous properties of mercaptans.

To render claims obvious, references must yield the claimed composition or method; they must satisfy all of the claim limitations and hence put the claimed invention in possession of the public. *In re Hoeksema*, 158 U.S.P.Q. 596 (C.C.P.A. 1968). Chiba in view of Ashurst does not put applicants' claimed invention in possession of the public, because it does not teach, suggest, or motivate the 3-mercaptoalkanoic acid esters in a flavor or fragrance composition, or a method of flavoring or fragrancng a product by adding the claimed composition.

The prior art must be analyzed in its entirety to determine if it renders the claimed invention, considered as a whole, obvious. *Loctite Corp. v. Ultraseal Ltd.*, 228 U.S.P.Q. 90 (Fed. Cir. 1985). The prior art must teach or suggest all of the claimed limitations; the ability to explain or reconstruct the invention from the references does not render the invention obvious. *Id.* One cannot pick and choose from references only what is needed to support a given position, and exclude other parts necessary to appreciate what the references as a whole suggest. *In re Wesslau*, 147 U.S.P.Q. 391 (C.C.P.A. 1965); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 230 U.S.P.Q. 416 (Fed. Cir. 1986). Nor can the claimed invention be merely inherent in the prior art. *In re Shetty* 195 U.S.P.Q. 753 (C.C.P.A. 1977). Even if the prior art may be modified, it

(that is, the prior art) must have suggested the desirability of the modification. *In re Gordon*, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984) ("The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification"). The references cited as rendering an invention obvious must, to a person of ordinary skill in the art, teach how to carry out the claimed process, and that there would be a reasonable expectation of success. *In re Vaeck*, 220 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success....Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure.

(p. 1442, internal cites omitted).

Chiba in view of Ashurst does not meet these standards for a *prima facie* case of obviousness.

Chiba, the primary reference, "relates to a process of preparing mercaptocarboxylic acid esters. Mercaptocarboxylic acid esters are useful as starting materials in the preparation of various industrial chemicals and, in particular, they can be reacted with alkyltin compounds to produce highly efficient stabilizers for synthetic resins" (Chiba column 1, lines 10-17). Chiba is non-analogous art to the claimed invention; the invention is a flavor or fragrance composition and its use for flavoring and

fragrancing products, containing known 3-mercaptoalkanoic acid esters not heretofore used for this purpose. In contrast, Chiba's preparation is directed to solving the problems of "high yield and ease of operation" (Chiba column 1, line 40 to column 2, line 45).

With respect to Ashurst, the secondary reference, the Examiner finds that it discloses mercaptans (compounds containing -SH) in general as food flavorings. However, there is absolutely no disclosure of the claimed 3-mercaptoalkanoic acid esters in flavoring or fragrancing compositions and methods. Indeed, Ashurst does not teach, suggest, or motivate the use of 3-mercaptoalkanoic acid esters at all.

The Examiner's combination of Chiba's compounds, based on Ashurst's "well-known use of mercaptans as flavoring agents" (Office Actions October 2, 2002, bottom of page 2; May 30, 2003, middle of page 2), is inapposite.

As known to one skilled in the art, most mercaptans have undesirable odors, and thus do not render obvious the claimed flavor or fragrance composition or method. The malodorous property of mercaptans is a defining characteristic (mercaptans hav[e] "a characteristically disagreeable odor" (McGraw-Hill Dictionary of Chemical Terms, McGraw-Hill Book Company, New York, page 259 (1984); "many are characterized by "strong and repulsive odors" (Hawley's Condensed Chemical Dictionary, Thirteenth Edition, Van Nostrand Reinhold, New York (1997), pages 709, 1100, relevant pages attached). A "disagreeable" or "repulsive" odor would clearly teach away from applicants' claimed compositions containing mercaptans as flavor or

fragrancing agent. This negates the Examiner's assertion that "It would have been obvious to a person of ordinary skill in the art, at the time the invention was made, to use the compounds of Chiba et al as flavorants, because the use of mercaptans as flavoring agents is conventional in the art, as taught by Ashurst" (Office Action October 2, 2002, top of page 3).

As applicants point out, the fact that these specific compounds imparted the desired clear fruity flavor properties was not obvious.

Surprisingly [the claimed compounds] overcome the aforementioned disadvantage of having the fruity note always combined with green and/or fatty notes, and, hence, can be used as flavor or fragrance compounds with a clear fresh character. Thus, the present invention is directed to this subject matter.

(page 5, lines 8-16). Even more surprising, further supporting the fact that these claimed compositions and methods were not obvious, was that the compounds themselves were known.

It has been found that the compounds of the present invention exhibit fruity properties, mainly in the range of passion fruit, cassis or tropical fruit. These organoleptic properties have never been described before, although the compounds themselves are already known, as previously stated.

(page 7 lines 12-16, emphasis added).

Applicants' examples further demonstrate the non-obviousness of the claimed invention. In Example 5, two structurally similar compounds, differing by only one carbon, were added to an orange

drink blank at identical concentrations. With only one carbon difference, dramatically different organoleptic properties resulted:

3-mercaptop <u>butanoic</u> acid methyl ester	strong fruity orange, mandarin, fresh squeezed note
3-mercaptop <u>hexanoic</u> acid methyl ester	strong fatty sulfury, woody, grapefruit aspect

3-mercaptophexanoic acid methyl ester was known in the prior art, and was the most structurally similar to the inventive composition (page 14, lines 6 to page 15, line 6).

Examples 6 and 7 (page 15, line 7 to page 18, line 13) similarly show dramatically different results from two structurally similar compounds. In Example 6, two compounds that differed by just two carbons, were added to a berry flavored yogurt blank:

3-mercaptop <u>butanoic</u> acid <u>ethyl</u> ester	change to blueberry flavor from blackberry; increased freshness
3-mercaptop <u>hexanoic</u> acid <u>methyl</u> ester	soapy, fatty, meaty, sulfur

In Example 7, two compounds that differed by just one carbon, were added to a clementine accord:

3-mercaptop <u>butanoic</u> acid methyl ester	enhanced natural clementine flavor sparkling, increased diffusivity
3-mercaptop <u>hexanoic</u> acid methyl ester	much less diffusivity fatty, meaty, sulfur

Such data amply show the unobviousness of the claimed 3-mercaptopalkanoic acid esters in flavor and fragrance compositions, which by definition impart a pleasing rather than an offensive taste/aroma.

Even if Chiba were combined with Ashurst, which there is no motivation to do as previously described, there is no reasonable expectation of success that it would yield the claimed invention of specific 3-mercaptoalkanoic acid esters for flavor or fragrance compositions. Ashurst itself teaches that mercaptans have a wide range of flavors ("The odour effect ranges from the simple unpleasant mercaptans (methyl mercaptan) through unsaturated short-chain garlic and onion compounds (allyl mercaptan, diallyl disulphide) to pleasant distinctly nuanced heterocyclic compounds" (page 155 bottom to page 156 top). There is simply no guidance given in Ashurst to select, among all mercaptans, the specific 3-mercaptoalkanoic acid esters that applicants' claim, particularly because Ashurst does not even suggest 3-mercaptoalkanoic acid esters in food flavoring.

In summary, Chiba discloses the synthesis, not the use, of mercaptocarboxylic acid esters. Ashurst discloses mercaptans in general as food flavorings, it does not disclose, teach, or suggest the specific 3-mercaptoalkanoic acid esters claimed. As analyzed, one skilled in the art cannot predict from the chemical structure which mercaptans may be useful in a flavor or fragrance composition, or in a method to flavor or fragrance a product, even when the mercaptans are structurally related (e.g., when they are all 3-mercapto alkanoic acid esters.) Applicants' invention is thus not obvious over Chiba in view of Ashurst, because Chiba is non-analogous art and thus is not a proper primary reference, there is no motivation to combine the references based on the references themselves or as known to one skilled in the art, and because there would not be a reasonable expectation of success for selecting the

specifically claimed 3-mercaptoalkanoic acid esters for their flavor and fragrance properties, as required for obviousness. Applicants respectfully assert that the Examiner has not met the basic requirements of a *prima facie* case of obviousness, as required under M.P.E.P. at 2143.

Summary

For the foregoing reasons, appellant believes that the Examiner's rejection of claims 1-16 was erroneous, and reversal of the decision is respectfully requested.

Enclosed is a check in the amount of \$330.00 for the filing of this Brief. Should any further fees be indicated herein, authorization is given to charge or credit any overpayment to Deposit Account No. 23-3000.

Respectfully submitted,

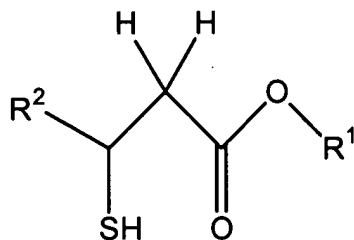
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APPENDIX A

1. A flavor or fragrance composition comprising at least one compound of formula I



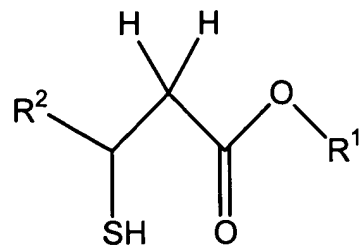
or a precursor thereof, wherein R¹ represents a branched or unbranched alkyl, alkenyl or alkadienyl group containing 1 to 8 carbon atoms and R² represents a methyl or ethyl group, in a flavor or fragrance composition.

2. The composition of claim 1 wherein R¹ is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, tert-butyl, n-hexyl, (Z)-2-hexenyl, (E)-3-hexenyl, (E)-2-hexenyl, (Z)-3-hexenyl and n-octyl.

3. The composition of claim 1 wherein at least one compound is selected from the group consisting of 3-mercaptopentanoic acid methyl ester, 3-mercaptopentanoic acid ethyl ester, 3-mercaptopentanoic acid n-hexyl ester, (R)-3-mercaptopentanoic acid methyl ester, 3-mercaptopentanoic acid (Z)-3-hexenyl ester, 3-mercaptopentanoic acid ethyl ester and precursors thereof.

4. The composition of claim 3 wherein at least one compound is selected from the group consisting of 3-mercaptoputanoic acid methyl ester and 3-mercaptoputanoic acid ethyl ester.
5. The composition of claim 1 wherein the total amount of carbon atoms of at least one compound of formula I is at least 8.
6. The composition of claim 1 wherein the precursor is formed by reaction of acyl chloride with the compound of formula 1.
7. The composition of claim 1 wherein the concentration of the compound of formula 1 or of the precursor thereof is from 0.001% to 30%.
8. The composition of claim 1 wherein the concentration of the compound of formula 1 or of the precursor thereof is from 0.001% to 10%.

9. A method of adding a flavor or fragrance to a product wherein at least one compound of formula 1



or a precursor thereof, wherein R1 represents a branched or unbranched alkyl, alkenyl or alkadienyl group containing 1 to 8 carbon atoms and R2 represents a methyl or an ethyl group, is added to the product for flavoring or fragrancng the product.

10. The method of claim 9 wherein the product is selected from the group consisting of a food, a beverage, a healthcare product, a household product, and combinations thereof.

11. The method of claim 9 wherein R1 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, -butyl, iso-butyl, tert-butyl, n-hexyl, (Z)-2-hexenyl, (E)-3-hexenyl, (E)-2-hexenyl, (Z)-3-hexenyl and n-octyl.

12. The method of claim 9 wherein at least one compound is selected from the group consisting of 3-mercaptoputanoic acid methyl ester, 3-mercaptoputanoic acid ethyl ester, 3-mercaptoputanoic acid n-hexyl ester, (R)-3-mercaptoputanoic acid methyl ester, 3-mercaptoputanoic acid (Z)-3-hexenyl ester, 3-mercaptopentanoic acid ethyl ester, and precursors thereof.

13. The method of claim 9 wherein at least one compound is selected from the group consisting of 3-mercaptoputanoic acid methyl ester and 3-mercaptoputanoic acid ethyl ester.

14. The method of claim 9 wherein the precursor is formed by reaction of acyl chloride with the compound of formula 1.

15. The method of claim 9 wherein the compound(s) of formula I or the precursor(s) thereof is/are present in an amount of 0.001 mg/kg to 500 mg/kg of said product.

16. The method of claim 9 wherein the compound(s) of formula I or the precursor(s) thereof is/are present in an amount of 0.01 mg/kg to 50 mg/kg of said product.

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Sybil P. Parker
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- menazon** $C_6H_8N_5O_2PS_2$ A colorless, crystalline compound that decomposes at 160–162°C; slightly soluble in water; used as an insecticide for the control of aphids. Also known as S-4,6-diamino-S-triazin-2-ylmethyl) O,O-dimethylphosphorodithioate.
- mendelevium** Synthetic radioactive element, symbol Md, with atomic number 101; made by bombarding lighter elements with light nuclei accelerated in cyclotrons.
- menthacampbor** See menthol.
- menthane** $C_{10}H_{20}$ A colorless water-insoluble liquid hydrocarbon; used in organic synthesis. Also known as hexahydrocymene; 4-isopropyl-1-methylcyclohexane; menthonaphthene; terpane.
- para-menthan-3-ol** See menthol.
- menthene** $C_{10}H_{18}$ A colorless, water-insoluble, liquid hydrocarbon; used in organic synthesis.
- menthol** $CH_3C_6H_6(C_3H_7)OH$ An alcohol-soluble, white crystalline compound that may exist in levo form or a mixture of dextro and levo isomers; used in medicines and perfumes, and as a flavoring agent. Also known as hexahydrothymol; 3-hydroxymenthane; menthacampbor; para-menthan-3-ol; methylhydroxyisopropylcyclohexane; peppermint camphor.
- menthonaphthene** See menthane.
- menthone** $C_{10}H_{18}O$ Oily, colorless ketonic liquid with slight peppermint odor; slightly soluble in water, soluble in organic solvents.
- menthyl** $C_{10}H_{19}$ A univalent radical that is derived from menthol by removal of the hydroxyl group.
- meperidine hydrochloride** $C_{15}H_{21}O_2N \cdot HCl$ A white, odorless crystalline compound, melting at 186–189°C; soluble in water and alcohol; used in medicine.
- mephentermine sulfate** $(C_{11}H_{17}N)_2 \cdot H_2SO_4 \cdot 2H_2O$ White odorless crystals; slightly soluble in alcohol, soluble in water; used in medicine.
- mephosfolan** $C_8H_{16}O_3PNS_2$ A yellow to amber liquid, used as an insecticide and miticide for agricultural crops.
- mepyrapone** See metyrapone.
- mer** A combining form denoting the repeating structure unit of any high polymer.
- merbromin** $C_{20}H_8O_6Na_2Br_2Hg$ A green crystalline powder that gives a deep-red solution in water; used as an antiseptic.
- mercamine** See 2-aminoethanethiol.
- mercapt-, mercapto-** A combining form denoting the presence of the thiol (SH) group.
- mercaptal** A group of organosulfur compounds that contain the group $=C(SR)_2$.
- mercaptamine** See 2-aminoethanethiol.
- mercaptan** A group of organosulfur compounds that are derivatives of hydrogen sulfide in the same way that alcohols are derivatives of water; have a characteristically disagreeable odor, and are found with other sulfur compounds in crude petroleum; an example is methyl mercaptan. Also known as thiol.
- mercaptide** A compound consisting of a metal and a mercaptan.
- mercaptoacetic acid** See thioglycollic acid.
- 2-mercaptobenzolic acid** See thiosalicylic acid.
- mercapt benzothiaz le** C_7H_5NS A yellow powder, melting at 164–174°C; used in rubber as a vulcanization accelerator with stearic acid. Also known as MBT.

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THIRTEENTH EDITION

Revised by

Richard J. Lewis, Sr.



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CIP

waste-liquor recovery, desalination, and electrolysis; processing whey proteins, biomedical research; gas separations, e.g., adjusting carbon monoxide/hydrogen ratios for ammonia production from synthesis gas; metal extraction and recovery. See osmosis; dialysis.

mentetrahdrophthalic anhydride. (methyl norbornene dicarboxylic anhydride).

CAS: 85-43-8. $C_7H_8O_3$.
Properties: Clear, transparent, slightly viscous liquid; colorless to light yellow.

Hazard: Strong irritant to eyes and skin.
Use: Curing epoxy resins, electrical laminating and filament winding, intermediate for polyesters, alkyl resins, and plasticizers.

MENA. Abbreviation for the methyl ester of naphthaleneacetic acid.

See α -naphthaleneacetic acid methyl ester.

menadione. (2-methyl-1,4-naphthoquinone; menaphthone; vitamin K₁).

CAS: 58-27-5. $C_{11}H_8O_2$.

Properties: Yellow, crystalline powder; nearly odorless. Mp 105–107°C. Affected by sunlight. Soluble in alcohol, benzene, and vegetable oils; insoluble in water.

Derivation: Oxidation of β -methylnaphthalene.

Grade: USP.

Hazard: Irritant to skin and mucous membranes, especially the alcoholic solution.

Use: Medicine, fungicides, animal feed additives.

menazon. (generic name for 5-[(4,6-diamino-5-triazin-2-yl)methyl]-O,O-dimethyl phosphorothioate).

CAS: 78-57-9.

$(CH_3O)_2P(S)CH_2C_6H_3N_4$.

Properties: Off-white solid. Mp 160–162°C. Slightly soluble in water and organic solvents.

Hazard: Highly toxic, cholinesterase inhibitor.

Use: Acaricide, insecticide.

mendelevium. Md. Synthetic radioactive element produced in a cyclotron by bombarding einsteinium with alpha particles; atomic number 101, aw 256, 4 isotopes, valence = 3. Mendelevium decays by spontaneous fission with a half-life of 1.5 hr. The heaviest isotope, Md-258, has a half-life of 60 days. Mendelevium is thought to have chemical properties similar to those of the rare earth thulium. It is made in research quantities only and no uses are reported.

See actinide series.

Mendeleyev, D. I. (1834–1907). Born in Siberia, Mendeleyev made a fundamental contribution to chemistry in 1869 by establishing the principle of periodicity of the elements. His first periodic table

was compiled on the basis of arranging the elements in ascending order of atomic weight and grouping them by similarity of properties. So accurate was Mendeleyev's thinking that he predicted the existence and atomic weights of several elements that were not actually discovered until years later. The original table has been modified and corrected several times, notably by Moseley, but it has accommodated the discovery of isotopes, rare gases, etc. Its importance in the development of chemical theory can hardly be overestimated. See Becquerel; Moseley; periodic table.

menhaden oil.

Properties: Yellowish-brown or reddish-brown, drying oil; characteristic odor. D 0.927–0.933, saponification value 191–196, iodine value 139–180, refr index 1.480. Soluble in ether, benzene, naphtha, and carbon disulfide. Combustible.

Derivation: By cooking or pressing the body of the menhaden fish.

Method of purification: Filtration and bleaching with fuller's earth.

Grade: Prime crude, brown, strained, bleached, winter oil, bleached winter white oil.

Hazard: Subject to spontaneous heating.
Use: Hydrogenated fats for cooking and industrial use (soap, rubber compounding), printing inks, animal feed, leather dressing lubricants, paint drier, cleansers, lipstick.

meniscus. The concave curve of a liquid surface in a graduate or narrow tube. Caused by surface tension. In reading a value (e.g., 5 cc), it is conventional to ignore the higher liquid around the perimeter. In the case of mercury, which does not wet the tube because of its extremely high surface tension, the meniscus is convex.

Menschutkin reaction. Reaction of tertiary amines with alkyl halides to form quaternary salts.

menthane-1,8-diamine. (p-menthane-1,8-diamine).

CAS: 80-52-4.

$(CH_3)_2C(NH_2)CH_2CH_2C(CH_3)(NH_2)CH_2CH_3$.

A primary alicyclic diamine, also a *tert*-alkylamine.

Properties: Clear liquid; terpene odor. Boiling range 107–126°C (10 mm Hg), bp –45°C, refr index 1.4794 (25°C). Miscible with water and most organic solvents.

Hazard: Strong irritant to eyes and skin, calls for eye protection.

Use: Curing agent for epoxy resins, chemical intermediate.

p-menthane-8-hydroperoxide.

CAS: 80-47-7. $C_{10}H_{18}O_2$.

Properties: Clear, pale-yellow liquid. D 0.910–0.925 (15.5/4°C), refr index 1.460–1.475 (20°C).

Hazard: Strong oxidizing agent, dangerous in contact with organic materials. Strong irritant to skin and eyes.

Use: Catalyst for rubber and polymerization reactions, coatings.

p-menthan-3-one. See menthone.

menthol. (hexahydrothymol; methylhydroxyisopropyl-cyclohexane; *p*-menthan-3-ol; peppermint camphor).

CAS: 89-78-1. $CH_3C_6H_4(C_3H_7)OH$. It may be *l*- (from natural sources) or *dl*- (natural or synthetic).

Properties: White crystals; cooling odor and taste. Mp 41–43°C (*l*-form), congealing temperature 27–28°C (*dl*-form), specific rotation –45 to –51 degrees (25°C) (*l*-menthol), –2 to +2 degrees (*dl*-menthol). Soluble in alcohol, light petroleum solvents, glacial acetic acid, and fixed or volatile oils; slightly soluble in water. Combustible.

Occurrence: Brazil (natural product), Japan.

Derivation: By freezing from peppermint oil, by hydrogenation of thymol.

Grade: Technical, USP, FCC.

Hazard: Irritant to mucous membranes on inhalation.

Use: Perfumery, cigarettes, liqueurs, flavoring agent, chewing gum, chest rubs, cough drops.

menthol acetic ester. See menthyl acetate.

menthol valerate. (menthyl isovalerate).

$(CH_3)_2CHCH_2COOC_4H_9$.

Properties: Colorless liquid; mild odor; cooling, faintly bitter taste. D 0.907 (15.4°C). Insoluble in water; soluble in alcohol, chloroform, ether, and oils.

Derivation: By action of valeric acid on menthol.

Use: Medicine, flavoring.

menthone. (p-menthan-3-one).

CAS: 1074-95-9. $C_{10}H_{18}O$.

Properties: Colorless, oily, mobile liquid; slight peppermint odor. D 0.897 (15°C), bp 207°C. Slightly soluble in water; soluble in organic solvents. Combustible.

Derivation: A ketone found in oil of peppermint.

Use: Flavoring.

menthyl acetate. (menthol acetic ester).

CAS: 16409-45-3. $C_{12}H_{22}O_2$.

Properties: Colorless liquid; menthollike odor. Bp 227–228°C, d 0.922–0.927, optical rotation –72 degrees 47 minutes to –73 degrees 18 minutes, refr index 1.447. Slightly soluble in water; miscible with alcohol and ether. Combustible.

Derivation: (1) By boiling menthol with acetic anhydride in the presence of sodium acetate; (2) peppermint oil.

Use: Perfumery, flavoring.

menthyl isovalerate. See menthol valerate.

menthyl salicylate. $C_6H_4(OH)COOC_6H_{13}$.

Properties: Colorless liquid. Miscible with alcohol, ether, chloroform, and fatty oils; insoluble in water; soluble in organic solvents. Combustible.

Use: Sunscreen preparations.

See homomenthyl salicylate.

MEP. Abbreviation for methyl ethyl pyridine.

meperidine hydrochloride. (Demerol).

CAS: 50-13-5. $C_{15}H_{21}NO_2 \cdot HCl$. An addictive drug, use by prescription only.

Use: Analgesic.

mepivacaine. (Carbocaine; 1-methyl-2-(2,6-dimethylcarbamoyl)piperidine).

Use: Local anesthetic.

meprobamate. (2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate).

CAS: 57-53-4.

Properties: White powder; characteristic odor; bitter taste. Mp 103–107°C. Slightly soluble in water and ether; soluble in alcohol and acetone.

Grade: NF.

Hazard: Central nervous system depressant, use restricted by law.

Use: Medicine (anxiolytic agent).

meq. Abbreviation for milliequivalent. See eq.

merbromin. (dibromohydroxymercurifluorescein disodium salt; 2,7-disodiumdibromo-4-hydroxymercurifluorescein).

CAS: 129-16-8. $C_{20}H_8Br_2HgNa_2O_6$.

Properties: Iridescent green scales or granules; odorless. Soluble in water; insoluble in alcohol, acetone, chloroform, or ether; stable in air.

Derivation: From dibromofluorescein and mercuric acetate.

Grade: Technical, NF.

Hazard: Toxic by ingestion. TLV (Hg): 0.05 mg/m³ of air.

Use: Medicine (antiseptic).

mercaptol process. Process of removing mercaptans from gasoline by counter-current liquid-liquid extraction with various liquids, as with a water solution of caustic soda and tar acids.

mercaptamine. See 2-aminoethanethiol.

mercaptan. See thiol.

mercaptoacetic acid. See thioglycolic acid.

Use: Intermediate for elastomers and antioxidants; solvent for dyes in textile printing.
See "Kromfax" [Alcolac].

thiodiglycolic acid.

CAS: 123-93-3. $\text{HOOCCH}_2\text{SCH}_2\text{COOH}$. A dicarboxylic acid.

Properties: Colorless crystals. Mp 128C. Soluble in water and alcohol. Combustible.

Use: Analytical reagent.

4'-thiodiphenol. (TDP). $(\text{C}_6\text{H}_4\text{OH})_2\text{S}$.

Properties: White, crystalline powder. Mp above 151C, 99.5% pure.

Use: Intermediate, flame-retardant, antioxidant, engineering plastics.

thiodiphenylamine. See phenothiazine.

thiodipropionic acid.

CAS: 111-17-1. $\text{HOOCCH}_2\text{CH}_2\cdot\text{S}\cdot\text{CH}_2\text{CH}_2\text{COOH}$. A dicarboxylic acid.

Properties: Leaflets. Mp 135. Soluble in water and alcohol.

Hazard: Use in foods restricted to 0.02% of fat and oil content, including essential oils.

Use: Antioxidant in food packaging, soaps, plasticizers, lubricants, fats, and oils.

3-thiodipropionitrile.

CAS: 111-97-7. $\text{S}(\text{CH}_2\text{CH}_2\text{CN})_2$.

Properties: White crystals or light-yellow liquid. D 1.1095 (30C), mp 28.65C. Slightly soluble in water and alcohol; soluble in acetone, chloroform, and benzene.

Use: Preservative, selective solvent, chromatography.

o-1,3-dithio[4,5-b]quinoxaline. See thioquinox.

ethanolamine. See 2-aminoethanethiol.

offlavine T. (CI 49005).

$\text{H}_3\text{C}_6\text{H}_3\text{N}(\text{HCl})\text{SCC}_6\text{H}_4\text{N}(\text{CH}_3)_2$.

Properties: A yellow basic dye of the thiazole class, fluoresces yellow to yellowish-green when excited by UV.

Derivation: By heating *p*-toluidine with sulfur in the presence of lead oxide.

Use: Textile dyeing, fluorescent sign paints, in combination with green or blue pigments to produce brilliant greens, phosphotungstic pigments.

thiofuran. See thiophene.

thioglycerol.

CAS: 96-27-5. $\text{CH}_2(\text{OH})\text{CH}(\text{OH})\text{CH}_2\text{SH}$.

Properties: Water-white liquid. Bp 118C (5 mm Hg), d 1.295 (14.4C). Soluble in water, alcohol, and ether. Combustible.

Use: Reducing agent for cystine molecule in human hair and wool, for stabilization of acrylonitrile polymers, medicine.

thioglycolic acid. (mercaptoacetic acid).

CAS: 68-11-1. HSCH_2COOH .

Properties: Colorless liquid; strong, unpleasant odor. D 1.325, fp -16.5C, bp 123C (29 mm Hg).

Miscible with water, alcohol, or ether. Combustible.

Derivation: Heating chloroacetic acid with potassium hydrogen sulfide.

Hazard: Toxic by ingestion and inhalation, strong irritant to tissue. TLV: 1 ppm in air.

Use: Reagent for iron, manufacture of thioglycolates, permanent-wave solutions and depilatories, vinyl stabilizer, manufacture of pharmaceuticals.

2-thiohydantoin. (glycolylthiourea).

$\text{NHC}(\text{S})\text{NHC}(\text{O})\text{CH}_2$.

Properties: Crystals or tan powder. Mp 230C. Slightly soluble in water; insoluble in alcohols and ethers.

Grade: 99% min.

Use: Intermediate for pharmaceuticals; rubber accelerators, copper-plating brighteners, and dye-stuffs.

2-thio-4-keto-thiazolidine. See rhodanine.

-thiol. (mercaptan). Suffix indicating that a substance belongs to the group of organic compounds resembling alcohols but having the oxygen of the hydroxyl group replaced by sulfur, as in ethanethiol ($\text{C}_2\text{H}_5\text{SH}$). Many thiols are characterized by strong and repulsive odors.

Hazard: Aliphatic thiols are flammable. Toxic by inhalation.

Use: Warning agents in fuel gas lines, chemical intermediates.

Note: Adoption of the name *thiol* to replace *mercaptan* has been officially approved as more consistent with the molecular constitution of these compounds. The older term, which literally means "mercury seizing," is inappropriate.

thiolactic acid. (2-mercaptopropionic acid).

CAS: 79-42-5. $\text{CH}_3\text{CH}(\text{SH})\text{COOH}$.

Properties: Oily liquid; unpleasant odor. Becomes crystalline at 10C, d 1.22, bp 116C (16 mm Hg), refr index 1.482. Soluble in water, alcohol, and acetone. Readily forms salts with numerous metals that have quite different properties.

Derivation: Reaction of sodium sulfide, sulfur, and bromopropionic acid.

Use: Depilatory, hair-waving preparations.

thiomalic acid. (mercaptosuccinic acid).

CAS: 70-49-5. $\text{HOOCCH}(\text{SH})\text{CH}_2\text{COOH}$.

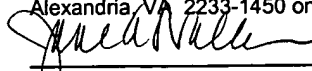
Properties: White crystals or powder; sulfuric odor. Mp 149-150C. Soluble in water, alcohol, acetone, and ether; slightly soluble in benzene. Combustible.



PATENT

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 2233-1450 on January 12, 2004


Jane A. Walker

January 12, 2004
Date

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex Parte Gassenmeier et al.
Appeal No. _____

Applicant: Gassenmeier et al.
Serial Number: 09/800,624
Filed: March 7, 2001
Confirmation No.: 7473
Art Unit: 1761
Examiner: Wong, Leslie A.
Title: **ORGANOLEPTIC COMPOSITIONS: USE OF 3-MERCAPTO
ALKANOIC ACID ESTERS AS FLAVOR INGREDIENTS**
Attorney Ref. No.: GRISA-710

Cincinnati, Ohio 45202

January 12, 2004

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

This is an appeal from the decision of the Examiner in a final Office Action dated May 19, 2003 (Paper No. 13). The pending rejected claims appear in the Appendix.

Real Party in Interest

The subject application is owned by Givaudan SA, Vernier, Switzerland.

Related Appeals and Interferences

None.

Status of the Claims

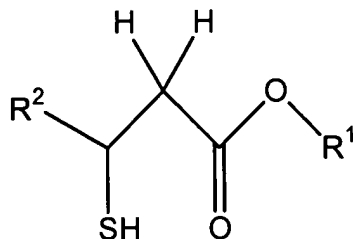
All pending claims 1-16 as listed in the Appendix are finally rejected under 35 U.S.C. § 103(a) over GB Patent 1 409 209 in view of Ashurst, Ed., Food Flavorings, Second edition, Blackie Academic & Professional, New York, 1995, pages 155-157. All pending claims 1-16 are appealed.

Status of Amendments

There are no amendments subsequent to the final office Action.

Summary of the Invention

A flavor or fragrance composition having at least one compound of formula I



which is a 3-mercaptoalkanoic acid ester, where R¹ is a branched or unbranched alkyl, alkenyl or alkadienyl group of C₁₋₈, and R² is methyl or ethyl, or a precursor, is disclosed (page 3, lines 9-14). Methods of flavoring or fragrancng products with these compositions are also disclosed (page 4, lines 8-15). While 3-mercaptoalkanoic acid

esters are known compounds (page 7, lines 4-11), their organoleptic properties had not previously been realized (page 7, lines 12-16). Thus, the claimed flavor or fragrance composition containing these specific 3-mercaptoalkanoic acid esters, and method of flavoring or fragrancng using the composition, was inventive (page 5, line 9 to page 6, line 1).

Issue

Whether claims 1-16 are obvious under 35 U.S.C. § 103(a) over GB Patent 1 409 209 (hereinafter referred to as "Chiba") in view of Ashurst, Ed., Food Flavorings, Second edition, Blackie Academic & Professional, New York, 1995, pages 155-157 (hereinafter referred to as "Ashurst").

Grouping of Claims

The rejected claims stand and fall together.

Argument

The Examiner finds that Chiba discloses the claimed compounds, but not the specific use of the compounds as flavoring agents. The Examiner finds Ashurst discloses the well-known use of mercaptans as flavoring agents, and that it would be obvious to one skilled in the art to use Chiba's compounds as flavorants because the use of mercaptans as flavoring agents is conventional, as Ashurst teaches.

Applicants disagree with the Examiner because (1) one skilled in the art of flavor or fragrance compositions and methods would not look to Chiba, which discloses a method of preparing mercaptocarboxylic acid esters for industrial synthesis starting materials; (2) there is no motivation to combine Chiba with Ashurst because Chiba does

not teach or suggest any flavor or fragrance properties of mercaptocarboxylic acid esters, while Ashurst does not teach or suggest 3-mercaptoalkanoic acid esters at all; and (3) even if Chiba were combined with Ashurst, there is no reasonable expectation of success that it would yield 3-mercaptoalkanoic acid ester flavor or fragrance compositions, one reason being the known malodorous properties of mercaptans.

To render claims obvious, references must yield the claimed composition or method; they must satisfy all of the claim limitations and hence put the claimed invention in possession of the public. *In re Hoeksema*, 158 U.S.P.Q. 596 (C.C.P.A. 1968). Chiba in view of Ashurst does not put applicants' claimed invention in possession of the public, because it does not teach, suggest, or motivate the 3-mercaptoalkanoic acid esters in a flavor or fragrance composition, or a method of flavoring or fragrancng a product by adding the claimed composition.

The prior art must be analyzed in its entirety to determine if it renders the claimed invention, considered as a whole, obvious. *Loctite Corp. v. Ultraseal Ltd.*, 228 U.S.P.Q. 90 (Fed. Cir. 1985). The prior art must teach or suggest all of the claimed limitations; the ability to explain or reconstruct the invention from the references does not render the invention obvious. *Id.* One cannot pick and choose from references only what is needed to support a given position, and exclude other parts necessary to appreciate what the references as a whole suggest. *In re Wesslau*, 147 U.S.P.Q. 391 (C.C.P.A. 1965); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 230 U.S.P.Q. 416 (Fed. Cir. 1986). Nor can the claimed invention be merely inherent in the prior art. *In re Shetty* 195 U.S.P.Q. 753 (C.C.P.A. 1977). Even if the prior art may be modified, it

(that is, the prior art) must have suggested the desirability of the modification. *In re Gordon*, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984) ("The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification"). The references cited as rendering an invention obvious must, to a person of ordinary skill in the art, teach how to carry out the claimed process, and that there would be a reasonable expectation of success. *In re Vaeck*, 220 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success....Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure.

(p. 1442, internal cites omitted).

Chiba in view of Ashurst does not meet these standards for a *prima facie* case of obviousness.

Chiba, the primary reference, "relates to a process of preparing mercaptocarboxylic acid esters. Mercaptocarboxylic acid esters are useful as starting materials in the preparation of various industrial chemicals and, in particular, they can be reacted with alkyltin compounds to produce highly efficient stabilizers for synthetic resins" (Chiba column 1, lines 10-17). Chiba is non-analogous art to the claimed invention; the invention is a flavor or fragrance composition and its use for flavoring and

fragrancing products, containing known 3-mercaptoalkanoic acid esters not heretofore used for this purpose. In contrast, Chiba's preparation is directed to solving the problems of "high yield and ease of operation" (Chiba column 1, line 40 to column 2, line 45).

With respect to Ashurst, the secondary reference, the Examiner finds that it discloses mercaptans (compounds containing –SH) in general as food flavorings. However, there is absolutely no disclosure of the claimed 3-mercaptoalkanoic acid esters in flavoring or fragranting compositions and methods. Indeed, Ashurst does not teach, suggest, or motivate the use of 3-mercaptoalkanoic acid esters at all.

The Examiner's combination of Chiba's compounds, based on Ashurst's "well-known use of mercaptans as flavoring agents" (Office Actions October 2, 2002, bottom of page 2; May 30, 2003, middle of page 2), is inapposite.

As known to one skilled in the art, most mercaptans have undesirable odors, and thus do not render obvious the claimed flavor or fragrance composition or method. The malodorous property of mercaptans is a defining characteristic (mercaptans hav[e] "a characteristically disagreeable odor" (McGraw-Hill Dictionary of Chemical Terms, McGraw-Hill Book Company, New York, page 259 (1984); "many are characterized by "strong and repulsive odors" (Hawley's Condensed Chemical Dictionary, Thirteenth Edition, Van Nostrand Reinhold, New York (1997), pages 709, 1100, relevant pages attached). A "disagreeable" or "repulsive" odor would clearly teach away from applicants' claimed compositions containing mercaptans as flavor or

fragrancing agent. This negates the Examiner's assertion that "It would have been obvious to a person of ordinary skill in the art, at the time the invention was made, to use the compounds of Chiba et al as flavorants, because the use of mercaptans as flavoring agents is conventional in the art, as taught by Ashurst" (Office Action October 2, 2002, top of page 3).

As applicants point out, the fact that these specific compounds imparted the desired clear fruity flavor properties was not obvious.

Surprisingly [the claimed compounds] overcome the aforementioned disadvantage of having the fruity note always combined with green and/or fatty notes, and, hence, can be used as flavor or fragrance compounds with a clear fresh character. Thus, the present invention is directed to this subject matter.

(page 5, lines 8-16). Even more surprising, further supporting the fact that these claimed compositions and methods were not obvious, was that the compounds themselves were known.

It has been found that the compounds of the present invention exhibit fruity properties, mainly in the range of passion fruit, cassis or tropical fruit. These organoleptic properties have never been described before, although the compounds themselves are already known, as previously stated.

(page 7 lines 12-16, emphasis added).

Applicants' examples further demonstrate the non-obviousness of the claimed invention. In Example 5, two structurally similar compounds, differing by only one carbon, were added to an orange

drink blank at identical concentrations. With only one carbon difference, dramatically different organoleptic properties resulted:

3-mercaptobutanoic acid methyl ester	strong fruity orange, mandarin, fresh squeezed note
3-mercaptohexanoic acid methyl ester	strong fatty sulfury, woody, grapefruit aspect

3-mercaptohexanoic acid methyl ester was known in the prior art, and was the most structurally similar to the inventive composition (page 14, lines 6 to page 15, line 6).

Examples 6 and 7 (page 15, line 7 to page 18, line 13) similarly show dramatically different results from two structurally similar compounds. In Example 6, two compounds that differed by just two carbons, were added to a berry flavored yogurt blank:

3-mercaptobutanoic acid ethyl ester	change to blueberry flavor from blackberry; increased freshness
3-mercaptohexanoic acid methyl ester	soapy, fatty, meaty, sulfur

In Example 7, two compounds that differed by just one carbon, were added to a clementine accord:

3-mercaptobutanoic acid methyl ester	enhanced natural clementine flavor sparkling, increased diffusivity
3-mercaptohexanoic acid methyl ester	much less diffusivity fatty, meaty, sulfur

Such data amply show the unobviousness of the claimed 3-mercaptoalkanoic acid esters in flavor and fragrance compositions, which by definition impart a pleasing rather than an offensive taste/aroma.

Even if Chiba were combined with Ashurst, which there is no motivation to do as previously described, there is no reasonable expectation of success that it would yield the claimed invention of specific 3-mercaptoalkanoic acid esters for flavor or fragrance compositions. Ashurst itself teaches that mercaptans have a wide range of flavors ("The odour effect ranges from the simple unpleasant mercaptans (methyl mercaptan) through unsaturated short-chain garlic and onion compounds (allyl mercaptan, diallyl disulphide) to pleasant distinctly nuanced heterocyclic compounds" (page 155 bottom to page 156 top). There is simply no guidance given in Ashurst to select, among all mercaptans, the specific 3-mercaptoalkanoic acid esters that applicants' claim, particularly because Ashurst does not even suggest 3-mercaptoalkanoic acid esters in food flavoring.

In summary, Chiba discloses the synthesis, not the use, of mercaptocarboxylic acid esters. Ashurst discloses mercaptans in general as food flavorings, it does not disclose, teach, or suggest the specific 3-mercaptoalkanoic acid esters claimed. As analyzed, one skilled in the art cannot predict from the chemical structure which mercaptans may be useful in a flavor or fragrance composition, or in a method to flavor or fragrance a product, even when the mercaptans are structurally related (e.g., when they are all 3-mercapto alkanoic acid esters.) Applicants' invention is thus not obvious over Chiba in view of Ashurst, because Chiba is non-analogous art and thus is not a proper primary reference, there is no motivation to combine the references based on the references themselves or as known to one skilled in the art, and because there would not be a reasonable expectation of success for selecting the

specifically claimed 3-mercaptoalkanoic acid esters for their flavor and fragrance properties, as required for obviousness. Applicants respectfully assert that the Examiner has not met the basic requirements of a *prima facie* case of obviousness, as required under M.P.E.P. at 2143.

Summary

For the foregoing reasons, appellant believes that the Examiner's rejection of claims 1-16 was erroneous, and reversal of the decision is respectfully requested.

Enclosed is a check in the amount of \$330.00 for the filing of this Brief. Should any further fees be indicated herein, authorization is given to charge or credit any overpayment to Deposit Account No. 23-3000.

Respectfully submitted,

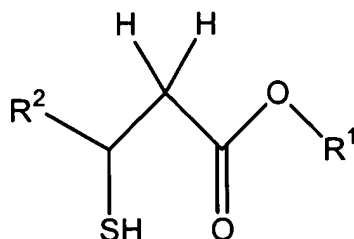
WOOD, HERRON & EVANS, L.L.P.

By Beverly A. Lyman
Beverly A. Lyman, Ph.D.
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APPENDIX A

1. A flavor or fragrance composition comprising at least one compound of formula I



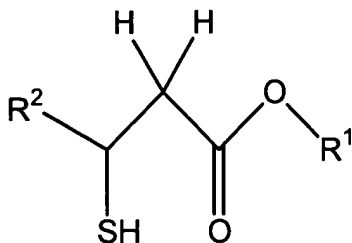
or a precursor thereof, wherein R¹ represents a branched or unbranched alkyl, alkenyl or alkadienyl group containing 1 to 8 carbon atoms and R² represents a methyl or ethyl group, in a flavor or fragrance composition.

2. The composition of claim 1 wherein R¹ is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, tert-butyl, n-hexyl, (Z)-2-hexenyl, (E)-3-hexenyl, (E)-2-hexenyl, (Z)-3-hexenyl and n-octyl.

3. The composition of claim 1 wherein at least one compound is selected from the group consisting of 3-mercaptobutanoic acid methyl ester, 3-mercaptobutanoic acid ethyl ester, 3-mercaptobutanoic acid n-hexyl ester, (R)-3-mercaptobutanoic acid methyl ester, 3-mercaptobutanoic acid (Z)-3-hexenyl ester, 3-mercaptopentanoic acid ethyl ester and precursors thereof.

4. The composition of claim 3 wherein at least one compound is selected from the group consisting of 3-mercaptoputanoic acid methyl ester and 3-mercaptoputanoic acid ethyl ester.
5. The composition of claim 1 wherein the total amount of carbon atoms of at least one compound of formula I is at least 8.
6. The composition of claim 1 wherein the precursor is formed by reaction of acyl chloride with the compound of formula 1.
7. The composition of claim 1 wherein the concentration of the compound of formula 1 or of the precursor thereof is from 0.001% to 30%.
8. The composition of claim 1 wherein the concentration of the compound of formula 1 or of the precursor thereof is from 0.001% to 10%.

9. A method of adding a flavor or fragrance to a product wherein at least one compound of formula 1



or a precursor thereof, wherein R1 represents a branched or unbranched alkyl, alkenyl or alkadienyl group containing 1 to 8 carbon atoms and R2 represents a methyl or an ethyl group, is added to the product for flavoring or fragrancng the product.

10. The method of claim 9 wherein the product is selected from the group consisting of a food, a beverage, a healthcare product, a household product, and combinations thereof.

11. The method of claim 9 wherein R1 is selected from the group consisting of methyl, ethyl, n-propyl, iso-propyl, -butyl, iso-butyl, tert-butyl, n-hexyl, (Z)-2-hexenyl, (E)-3-hexenyl, (E)-2-hexenyl, (Z)-3-hexenyl and n-octyl.

12. The method of claim 9 wherein at least one compound is selected from the group consisting of 3-mercaptoputanoic acid methyl ester, 3-mercaptoputanoic acid ethyl ester, 3-mercaptoputanoic acid n-hexyl ester, (R)-3-mercaptoputanoic acid methyl ester, 3-mercaptoputanoic acid (Z)-3-hexenyl ester, 3-mercaptopentanoic acid ethyl ester, and precursors thereof.

13. The method of claim 9 wherein at least one compound is selected from the group consisting of 3-mercaptoputanoic acid methyl ester and 3-mercaptoputanoic acid ethyl ester.

14. The method of claim 9 wherein the precursor is formed by reaction of acyl chloride with the compound of formula 1.

15. The method of claim 9 wherein the compound(s) of formula I or the precursor(s) thereof is/are present in an amount of 0.001 mg/kg to 500 mg/kg of said product.

16. The method of claim 9 wherein the compound(s) of formula I or the precursor(s) thereof is/are present in an amount of 0.01 mg/kg to 50 mg/kg of said product.

McGraw-Hill Dictionary of **CHEMICAL TERMS**

Sybil P. Parker
EDITOR IN CHIEF

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On the cover: Photomicrograph of potassium nitrate under high pressure, a specimen contained in a diamond-anvil high-pressure cell. (National Bureau of Standards)

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menazon $C_6H_8N_5O_2PS_2$ A colorless, crystalline compound that decomposes at 160–162°C; slightly soluble in water; used as an insecticide for the control of aphids. Also known as S-4,6-diamino-S-triazin-2-ylmethyl) O,O-dimethylphosphorodithioate.

mendelevium Synthetic radioactive element, symbol Md, with atomic number 101; made by bombarding lighter elements with light nuclei accelerated in cyclotrons.

menthacampbor See menthol.

menthane $C_{10}H_{20}$ A colorless water-insoluble liquid hydrocarbon; used in organic synthesis. Also known as hexahydrocymene; 4-isopropyl-1-methylcyclohexane; menthonaphthene; terpane.

para-menthan-3-ol See menthol.

menthene $C_{10}H_{18}$ A colorless, water-insoluble, liquid hydrocarbon; used in organic synthesis.

menthol $CH_3C_6H_9(C_3H_7)OH$ An alcohol-soluble, white crystalline compound that may exist in levo form or a mixture of dextro and levo isomers; used in medicines and perfumes, and as a flavoring agent. Also known as hexahydrothymol; 3-hydroxy-menthane; menthacampbor; *para*-menthan-3-ol; methylhydroxyisopropylcyclohexane; peppermint camphor.

menthonaphthene See menthane.

menthone $C_{10}H_{18}O$ Oily, colorless ketonic liquid with slight peppermint odor; slightly soluble in water, soluble in organic solvents.

menthyl $C_{10}H_{19}$ A univalent radical that is derived from menthol by removal of the hydroxyl group.

meperidine hydrochloride $C_{15}H_{21}O_2N \cdot HCl$ A white, odorless crystalline compound, melting at 186–189°C; soluble in water and alcohol; used in medicine.

mephentermine sulfate $(C_{11}H_{17}N)_2 \cdot H_2SO_4 \cdot 2H_2O$ White odorless crystals; slightly soluble in alcohol, soluble in water; used in medicine.

mephosfolan $C_6H_{16}O_3PNS_2$ A yellow to amber liquid, used as an insecticide and miticide for agricultural crops.

mepyrapone See metyrapone.

-mer A combining form denoting the repeating structure unit of any high polymer.

merbromin $C_{20}H_8O_6Na_2Br_2Hg$ A green crystalline powder that gives a deep-red solution in water; used as an antiseptic.

mercamine See 2-aminoethanethiol.

mercapt-, mercapto- A combining form denoting the presence of the thiol (SH) group.

mercaptal A group of organosulfur compounds that contain the group $=C(SR)_2$.

mercaptamine See 2-aminoethanethiol.

mercaptan A group of organosulfur compounds that are derivatives of hydrogen sulfide in the same way that alcohols are derivatives of water; have a characteristically disagreeable odor, and are found with other sulfur compounds in crude petroleum; an example is methyl mercaptan. Also known as thiol.

mercaptide A compound consisting of a metal and a mercaptan.

mercaptoacetic acid See thioglycollic acid.

2-mercaptobenzoic acid See thiosalicylic acid.

mercaptobenzothiazole C_7H_5NS A yellow powder, melting at 164–174°C; used in rubber as a vulcanization accelerator with stearic acid. Also known as MBT.

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Dictionary

THIRTEENTH EDITION

Revised by

Richard J. Lewis, Sr.



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waste-liquor recovery, desalination, and electrolysis; processing whey proteins, biomedical research; gas separations, e.g., adjusting carbon monoxide/hydrogen ratios for ammonia production from synthesis gas; metal extraction and recovery.
See osmosis; dialysis.

mentetraphydrophthalic anhydride. (methyl norbornene dicarboxylic anhydride).

CAS: 85-43-8. $C_{10}H_{16}O_5$.
Properties: Clear, transparent, slightly viscous liquid; colorless to light yellow.
Hazard: Strong irritant to eyes and skin.
Use: Curing epoxy resins, electrical laminating and filament winding, intermediate for polyesters, alkyl resins, and plasticizers.

MENA. Abbreviation for the methyl ester of naphthaleneacetic acid.

See α -naphthaleneacetic acid methyl ester.

menadione. (2-methyl-1,4-naphthoquinone; menaphthone; vitamin K₃).

CAS: 58-27-5. $C_{11}H_8O_2$.
Properties: Yellow, crystalline powder; nearly odorless. Mp 105–107°C. Affected by sunlight. Soluble in alcohol, benzene, and vegetable oils; insoluble in water.
Derivation: Oxidation of β -methylnaphthalene.
Grade: USP.

Hazard: Irritant to skin and mucous membranes, especially the alcoholic solution.
Use: Medicine, fungicides, animal feed additives.

menazon. (generic name for S-[4-(6-diamino-5-triazin-2-yl)methyl]-O-D-dimethyl phosphorothioate).

CAS: 78-57-9.

$(CH_3O)_2P(S)SCH_2C_6H_4NC(NH_2)_2N$.
Properties: Off-white solid. Mp 160–162°C. Slightly soluble in water and organic solvents.
Hazard: Highly toxic, cholinesterase inhibitor.
Use: Acaricide, insecticide.

mendelevium. Md. Synthetic radioactive element produced in a cyclotron by bombarding einsteinium with alpha particles; atomic number 101, aw 256, 4 isotopes, valence = 3. Mendelevium decays by spontaneous fission with a half-life of 1.5 hr. The heaviest isotope, Md-258, has a half-life of 60 days. Mendelevium is thought to have chemical properties similar to those of the rare earth thulium. It is made in research quantities only and no uses are reported.

See actinide series.

Mendeleyev, D. I. (1834–1907). Born in Siberia, Mendeleyev made a fundamental contribution to chemistry in 1869 by establishing the principle of periodicity of the elements. His first periodic table

was compiled on the basis of arranging the elements in ascending order of atomic weight and grouping them by similarity of properties. So accurate was Mendeleyev's thinking that he predicted the existence and atomic weights of several elements that were not actually discovered until years later. The original table has been modified and corrected several times, notably by Moseley, but it has accommodated the discovery of isotopes, rare gases, etc. Its importance in the development of chemical theory can hardly be overestimated.
See Becquerel; Moseley; periodic table.

menhaden oil.

Properties: Yellowish-brown or reddish-brown, drying oil, characteristic odor. D 0.927–0.933, saponification value 191–196, iodine value 139–180, refr index 1.480. Soluble in ether, benzene, naphtha, and carbon disulfide. Combustible.

Derivation: By cooking or pressing the body of the menhaden fish.
Method of purification: Filtration and bleaching with fuller's earth.

Grade: Prime crude, brown, strained, bleached, winter oil, bleached winter white oil.
Hazard: Subject to spontaneous heating.
Use: Hydrogenated fats for cooking and industrial use (soap, rubber compounding), printing inks, animal feed, leather dressing lubricants, paint drier, cleansers, lipstick.

meniscus. The concave curve of a liquid surface in a graduate or narrow tube. Caused by surface tension. In reading a value (e.g., 5 cc), it is conventional to ignore the higher liquid around the perimeter. In the case of mercury, which does not wet the tube because of its extremely high surface tension, the meniscus is convex.

Menschutkin reaction. Reaction of tertiary amines with alkyl halides to form quaternary salts.

menthanediamine. (p-menthane-1,8-diamine).

CAS: 80-52-4.

$(CH_3)_2C(NH_2)CH_2CH_2C(CH_3)(NH_2)CH_2CH_3$.
A primary alicyclic diamine, also a *tert*-alkylamine.

Properties: Clear liquid; terpene odor. Boiling range 107–126°C (10 mm Hg), bp –45°C, refr index 1.4794 (25°C). Miscible with water and most organic solvents.

Hazard: Strong irritant to eyes and skin, calls for eye protection.
Use: Curing agent for epoxy resins, chemical intermediate.

P-menthane-8-hydroperoxide.

CAS: 80-47-7. $C_{10}H_{18}O_2$.

Properties: Clear, pale-yellow liquid. D 0.910–0.925 (15.5/4°C), refr index 1.460–1.475 (20°C).

Hazard: Strong oxidizing agent, dangerous in contact with organic materials. Strong irritant to skin and eyes.

Use: Catalyst for rubber and polymerization reactions, coatings.

p-menthan-3-one. See menthone.

menthol. (hexahydrothymol; methylhydroxyisopropyl-cyclohexane; p-menthan-3-ol; peppermint camphor).

CAS: 89-78-1. $CH_3C_6H_4(C_3H_7)OH$. It may be l- (from natural sources) or dl- (natural or synthetic). Properties: White crystals; cooling odor and taste. Mp 41–43°C (l-form), congealing temperature 27–28°C (dl-form), specific rotation –45 to –51 degrees (25°C) (l-menthol), –2 to +2 degrees (dl-menthol). Soluble in alcohol, light petroleum solvents, glacial acetic acid, and fixed or volatile oils; slightly soluble in water. Combustible.

Occurrence: Brazil (natural product), Japan.
Derivation: By freezing from peppermint oil, by hydrogenation of thymol.

Grade: Technical, USP, FCC.

Hazard: Irritant to mucous membranes on inhalation.
Use: Perfumery, cigarettes, liqueurs, flavoring agent, chewing gum, chest rubs, cough drops.

menthol acetic ester. See menthyl acetate.

menthol valerate. (menthyl isovalerate).

$(CH_3)_2CHCH_2COOC_4H_9$.
Properties: Colorless liquid; mild odor; cooling, faintly bitter taste. D 0.907 (15.4°C). Insoluble in water; soluble in alcohol, chloroform, ether, and oils.
Derivation: By action of valeric acid on menthol.

Use: Medicine, flavoring.

menthone. (p-menthan-3-one).

CAS: 1074-95-9. $C_{10}H_{18}O$.
Properties: Colorless, oily, mobile liquid; slight peppermint odor. D 0.897 (15°C), bp 207°C. Slightly soluble in water; soluble in organic solvents. Combustible.

Derivation: A ketone found in oil of peppermint.
Use: Flavoring.

menthyl acetate. (menthol acetic ester).

CAS: 16409-45-3. $C_{10}H_{18}OOCCH_3$.
Properties: Colorless liquid; menthol-like odor. Bp 227–228°C, d 0.922–0.927, optical rotation –72 degrees 47 minutes to –73 degrees 18 minutes, refr index 1.447. Slightly soluble in water; miscible with alcohol and ether. Combustible.

Derivation: (1) By boiling menthol with acetic anhydride in the presence of sodium acetate; (2) peppermint oil.
Use: Perfumery, flavoring.

menthyl isovalerate. See menthol valerate.

menthyl salicylate. $C_9H_{10}(OH)COOC_6H_4$.

Properties: Colorless liquid. Miscible with alcohol, ether, chloroform, and fatty oils; insoluble in water; soluble in organic solvents. Combustible.

Use: Sunscreen preparations.
See homomenthyl salicylate.

MEP. Abbreviation for methyl ethyl pyridine.

meperidine hydrochloride. (Demerol).

CAS: 50-13-5. $C_{17}H_{19}NO_3 \cdot HCl$. An addictive drug, use by prescription only.
Use: Analgesic.

mepivacaine. (Carbocaine; 1-methyl-2-(2,6-xylylcarbamoyl)piperidine).

Use: Local anesthetic.

meprobamate. (2-methyl-2-n-propyl-1,3-propanediol dicarbamate).

CAS: 57-53-4.
 $H_2NCOOCH_2C(CH_3)(C_2H_5)CH_2OOCNH_2$.
Properties: White powder; characteristic odor; bitter taste. Mp 103–107°C. Slightly soluble in water and ether; soluble in alcohol and acetone.

Grade: NF.

Hazard: Central nervous system depressant, use restricted by law.

Use: Medicine (anxiolytic agent).

meq. Abbreviation for milliequivalent. See eq.

merbromin. (dibromohydroxymercurifluorescein disodium salt; 2,7-disodiumdibromo-4-hydroxymercurifluorescein).

CAS: 129-16-8. $C_{20}H_8Br_2HgNa_2O_4$.
Properties: Iridescent green scales or granules; odorless. Soluble in water; insoluble in alcohol, acetone, chloroform, or ether; stable in air.

Derivation: From dibromofluorescein and mercuric acetate.

Grade: Technical, NF.

Hazard: Toxic by ingestion. TLV (Hg): 0.05 mg/m³ of air.

Use: Medicine (antiseptic).

mercaptol process. Process of removing mercaptans from gasoline by counter-current liquid-liquid extraction with various liquids, as with a water solution of caustic soda and tar acids.

mercaptamine. See 2-aminocethanethiol.

mercaptan. See thiol.

mercaptoacetic acid. See thioglycolic acid.

Use: Intermediate for elastomers and antioxidants; solvent for dyes in textile printing.
See "Kromfax" [Alcolac].

thiodiglycolic acid.

CAS: 123-93-3. $\text{HOOCCH}_2\text{SCH}_2\text{COOH}$. A dicarboxylic acid.

Properties: Colorless crystals. Mp 128C. Soluble in water and alcohol. Combustible.

Use: Analytical reagent.

4'-thiodiphenol. (TDP). $(\text{C}_6\text{H}_5\text{OH})_2\text{S}$.

Properties: White, crystalline powder. Mp above 151C, 99.5% pure.

Use: Intermediate, flame-retardant, antioxidant, engineering plastics.

thiodiphenylamine. See phenothiazine.

thiodipropionic acid.

CAS: 111-17-1. $\text{HOOCCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{COOH}$. A dicarboxylic acid.

Properties: Leaflets. Mp 135. Soluble in water and alcohol.

Hazard: Use in foods restricted to 0.02% of fat and oil content, including essential oils.

Use: Antioxidant in food packaging, soaps, plasticizers, lubricants, fats, and oils.

3-thiodipropionitrile.

CAS: 111-97-7. $\text{S}(\text{CH}_2\text{CH}_2\text{CN})_2$.

Properties: White crystals or light-yellow liquid. D 1.1095 (30C), mp 28.65C. Slightly soluble in water and alcohol; soluble in acetone, chloroform, and benzene.

Use: Preservative, selective solvent, chromatography.

o-1,3-dithio[4,5-b]quinoxaline. See thioquinox.

oethanolamine. See 2-aminoethanethiol.

offlavine T. (CI 49005).

$\text{H}_3\text{C}_6\text{H}_3\text{N}(\text{HCl})\text{SCC}_6\text{H}_4\text{N}(\text{CH}_3)_2$.

Properties: A yellow basic dye of the thiazole class, fluoresces yellow to yellowish-green when excited by UV.

Derivation: By heating *p*-toluidine with sulfur in the presence of lead oxide.

Use: Textile dyeing, fluorescent sign paints, in combination with green or blue pigments to produce brilliant greens, phosphotungstic pigments.

thiofuran. See thiophene.

thioglycerol.

CAS: 96-27-5. $\text{CH}_2(\text{OH})\text{CH}(\text{OH})\text{CH}_2\text{SH}$.

Properties: Water-white liquid. Bp 118C (5 mm Hg), d 1.295 (14.4C). Soluble in water, alcohol, and ether. Combustible.

Use: Reducing agent for cystine molecule in human hair and wool, for stabilization of acrylonitrile polymers, medicine.

thioglycolic acid. (mercaptoacetic acid).

CAS: 68-11-1. HSCH_2COOH .

Properties: Colorless liquid; strong, unpleasant odor. D 1.325, fp -16.5C, bp 123C (29 mm Hg).

Miscible with water, alcohol, or ether. Combustible.

Derivation: Heating chloroacetic acid with potassium hydrogen sulfide.

Hazard: Toxic by ingestion and inhalation, strong irritant to tissue. TLV: 1 ppm in air.

Use: Reagent for iron, manufacture of thioglycolates, permanent-wave solutions and depilatories, vinyl stabilizer, manufacture of pharmaceuticals.

2-thiohydantoin. (glycolylthiourea).

$\text{NHC}(\text{S})\text{NHC}(\text{O})\text{CH}_2$.

Properties: Crystals or tan powder. Mp 230C.

Slightly soluble in water; insoluble in alcohols and ethers.

Grade: 99% min.

Use: Intermediate for pharmaceuticals, rubber accelerators, copper-plating brighteners, and dye-stuffs.

2-thio-4-keto-thiazolidine. See rhodanine.

-thiol. (mercaptan). Suffix indicating that a substance belongs to the group of organic compounds resembling alcohols but having the oxygen of the hydroxyl group replaced by sulfur, as in ethanethiol ($\text{C}_2\text{H}_5\text{SH}$). Many thiols are characterized by strong and repulsive odors.

Hazard: Aliphatic thiols are flammable. Toxic by inhalation.

Use: Warning agents in fuel gas lines, chemical intermediates.

Note: Adoption of the name *thiol* to replace *mercaptan* has been officially approved as more consistent with the molecular constitution of these compounds. The older term, which literally means "mercury seizing," is inappropriate.

thiolactic acid. (2-mercaptopropionic acid).

CAS: 79-42-5. $\text{CH}_3\text{CH}(\text{SH})\text{COOH}$.

Properties: Oily liquid; unpleasant odor. Becomes crystalline at 10C, d 1.22, bp 116C (16 mm Hg), refr index 1.482. Soluble in water, alcohol, and acetone. Readily forms salts with numerous metals that have quite different properties.

Derivation: Reaction of sodium sulfide, sulfur, and bromopropionic acid.

Use: Depilatory, hair-waving preparations.

thiomalic acid. (mercaptosuccinic acid).

CAS: 70-49-5. $\text{HOOCCH}(\text{SH})\text{CH}_2\text{COOH}$.

Properties: White crystals or powder; sulfuric odor. Mp 149-150C. Soluble in water, alcohol, acetone, and ether; slightly soluble in benzene. Combustible.